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# Ultrasound Promoted Wurtz Coupling of Alkyl Bromides and Dibromides

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## Abstract

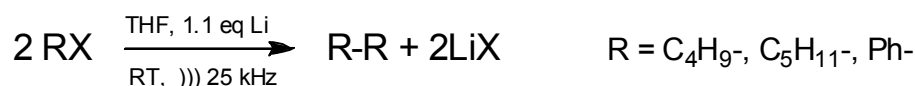
Sonochemically enhanced Wurtz coupling using lithium metal has been investigated for a number of isomeric alkyl bromides under a variety conditions. The products result from direct coupling of short lived radicals formed at the metal surface rather than the secondary radicals which can be formed during coupling of aromatic halides and thus give rise to a single major product. Coupling has been extended to dibrominated aryl and alkyl compounds as well as showing that aryl-alkyl coupling is possible. Dibrominated alkyls were found to give low molecular weight oligomers although no reaction occurred for 1,2- isomers. The growth of oligomers in THF may be solubility limited. A simple model is proposed to explain these findings.

**Keywords:** Ultrasound, sonochemistry, Wurtz coupling, lithium, bromoalkanes

## 1. Introduction

High intensity ultrasound is a useful tool for the acceleration of many synthetically useful organic and organometallic reactions. [1-3] A wide range of processes can be promoted and commonly reported effects include significant increases in rates and yields as well as, in some cases, an apparent switch in products due to the promotion of one possible mechanism in preference to others. [4, 5]

Among the heterogeneous reactions promoted by ultrasound is Wurtz-type coupling over reactive metals such as lithium (Scheme 1). Han and Boudjouk were the first to apply ultrasound to this reaction and reported the coupling between chloro-, bromo- and iodobenzene to form biphenyl in good yields [6] while the coupling of tolyl systems gave lower yields.



**Scheme 1.** Sonochemical Wurtz coupling

In related work, Osborne *et al.* [7] reported that coupling bromopyridines gave mixtures of isomeric bipyridyls and that dehalogenation to form pyridine was a major side reaction, indicating that the mechanism for aryl Wurtz coupling was more complex than first assumed. This was confirmed by Price and Clifton [8] who found that reaction of bromotoluenes also gave a mixture of products. Coupling of 2-bromotoluene yielded a mixture of 2,2-, 2,3- and 2,4 dimethyl biphenyl. Similarly, coupling of the 3- and 4-substituted isomers also gave mixtures in which one ring retained the methyl group in the original position of substitution while the other ring contained each of the three possible positions. They also found that these reactions were inhibited by a free radical scavenger, indicating that the coupling reaction involved a pathway involving free radical intermediates.

In addition to organic synthesis, ultrasound has also been applied to the preparation of polymers with controlled structures [9]. Among these, Wurtz type coupling reactions using sodium of dialkyl- and diaryl silanes has been used to prepare long chain poly(organosilanes) [10, 11, 12], polymers with all silicon backbones, and the reaction has also been applied to polymers made with tin backbones [13]. However, it has not previously been applied to carbon compounds, presumably due to their lower reactivity. Coupling dibromoalkanes containing branched alkyl groups offers the potential for forming polyolefins with controlled short-chain branches although further detail on the products and reaction mechanism is needed in order to evaluate the potential of this reaction. As far as we are aware, to date the

Wurtz type coupling of halogenoalkanes has only been studied for 1-chloropropane [6] and 1-bromobutane [14]. We therefore present here an investigation into the coupling of bromopentane isomers. In addition we have extended the ultrasonic Wurtz coupling reaction to dibromo aryl and alkyl systems to investigate the possibility of the formation of polymers with controlled branched structures.

## 2. Experimental

*Materials:* All reagents were used as received from Sigma Aldrich (UK) or Alfa Aesar (UK). Solvents used were of HPLC grade and used without further purification. Gases were obtained from BOC and were used without further purification.

*Instrumentation:* Gas chromatographic analysis was carried out using an Agilent 6890N Network gas chromatograph fitted with an HP-5 column. For bromobenzene analysis the initial temperature for the oven was 70 °C. This was held for 1 minute and then increased at 16 °C min<sup>-1</sup> to 150 °C. For analysis of bromopentanes, the initial oven temperature was 40 °C held for 5 min then increased at 16 °C min<sup>-1</sup> to 150 °C. <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> solution using a 300 MHz Bruker AV NMR spectrometer. <sup>1</sup>H NMR were recorded using a 250 MHz Bruker AV NMR spectrometer. Chemical shifts are reported with reference to TMS. Gel permeation chromatography was carried out using a Polymer Laboratories PL-GPC-50 Plus equipped with a PLGel 5µm “mixed C” column. THF was used as the eluting solvent at a flow rate of 1 cm<sup>3</sup> min<sup>-1</sup> at 30 °C.

*Sonication:* Reactions were carried out in a Kerry Ultrasound cleaning bath operating at 25 kHz delivering 0.4 W of power into the reaction, measured calorimetrically in the usual manner [15].

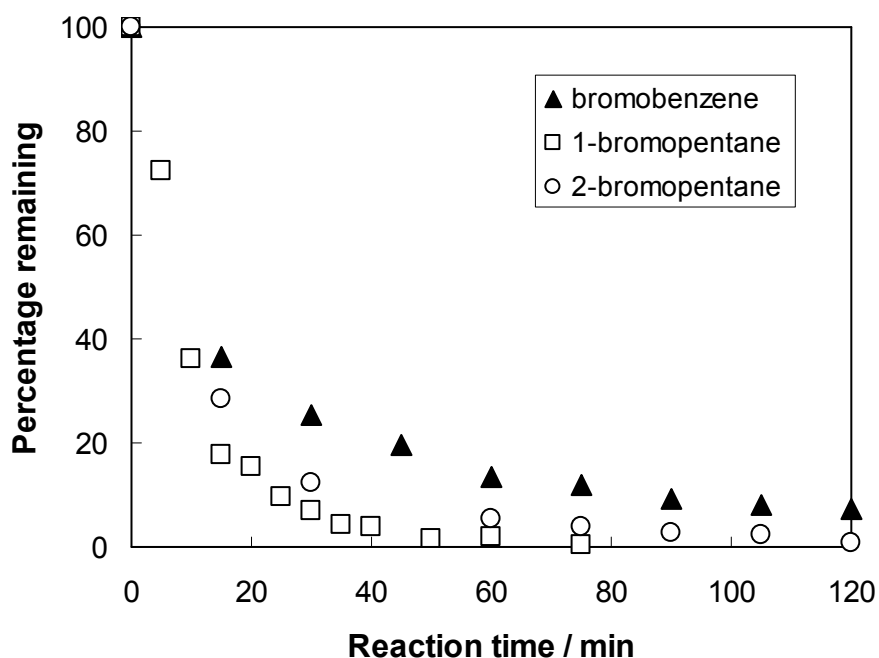
*Coupling of bromobenzene and bromopentanes:* In a 100 cm<sup>3</sup> conical flask with a ground glass neck joint, 10 mmol of brominated compound was dissolved in 25 cm<sup>3</sup> THF. To this was added 200 µL of dihexylether as an internal standard for GC analysis. The solution was purged with nitrogen for 10 minutes after which time 12 mmol (1.1 eq, 83 mg) of lithium pellets were added and the flask placed in the sonic bath so that the disturbance of the solution's surface by ultrasonic action was maximised. The samples were then sonicated while a slow flow of nitrogen was maintained. The solutions were sampled regularly taking 0.5 cm<sup>3</sup> aliquots which were diluted to 1 cm<sup>3</sup> with THF before injection into the GC.

*Coupling of dibrominated compounds:* The same method was used except that 2.2 equivalents of lithium were used and no dihexylether was added. After sonication the

residues were poured into 200 cm<sup>3</sup> of distilled water and the product extracted with two 100 cm<sup>3</sup> portions of diethyl ether. The organic layers were combined and dried using MgSO<sub>4</sub> before removing the solvent under vacuum.

### 3. Results and discussion

The reaction time for the sonochemical Wurtz coupling of bromobenzene has previously been reported as ranging between two and ten hours [6 - 8, 14]. Under the conditions used in this work, the reaction was essentially complete with respect to bromobenzene consumption after 2 hours, as shown in Figure 1. As previously reported, the only product recovered was biphenyl with a yield of approximately 70%. The remaining product is assumed to be benzene, resulting from a competitive dehalogenation reaction.



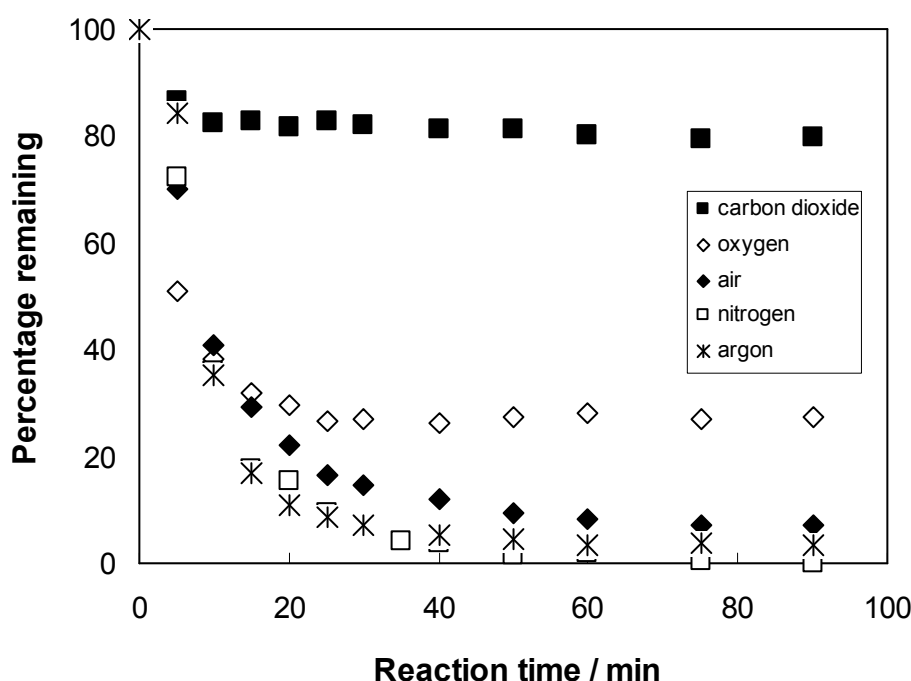
**Figure 1:** Consumption of bromobenzene and bromopentanes during sonochemical Wurtz coupling using lithium.

1-bromopentane was chosen for an initial study the reaction of alkyl bromides. The consumption of 1-bromopentane is also shown in Figure 1 and indicates a significantly faster reaction than with bromobenzene with complete consumption after around 40 min. The product was confirmed to be *n*-decane by comparison via GC and <sup>1</sup>H NMR with an authentic sample. The yield was 83% by <sup>1</sup>H NMR. No significant amounts of other products were

detected via GC or NMR. The consumption of 2-bromopentane was also faster than bromobenzene although somewhat slower than the 1- isomer.

The Wurtz coupling of bromoaryls is known to follow a mechanism involving radicals [6]. To investigate this for bromoalkyls, the reaction was repeated in the presence of excess DPPH, a free radical scavenger. After 2 hours of sonication, little of the 1-bromopentane had reacted (from GC analysis) and no coupling products were observed, confirming that radical intermediates were also involved in the reaction of alkyl bromides.

The coupling of 1-bromopentane was then studied under varying atmospheres. Figure 2 shows that the rate of reaction was similar under Argon and N<sub>2</sub>. The rate of consumption was somewhat slower under air but was essentially complete after 90 minutes. The rate was slower under O<sub>2</sub> and went to only 73% completion. Under CO<sub>2</sub> the reaction stopped after 15 minutes at a conversion of only 21%. The major product in each reaction was *n*-decane and for the reaction with CO<sub>2</sub> no products arising from CO<sub>2</sub> insertion were seen.

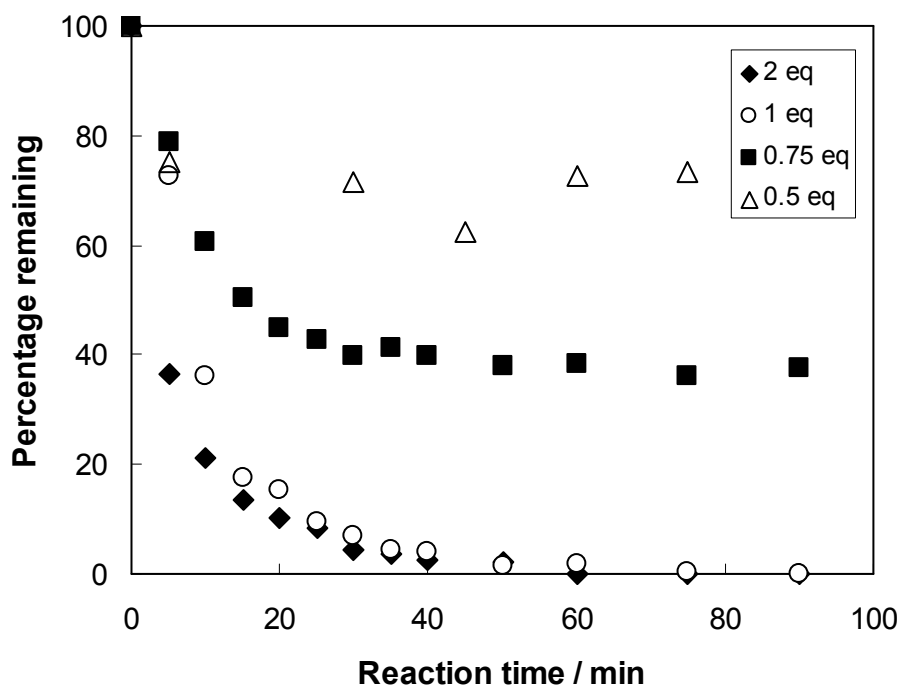


**Figure 2.** Effect of gaseous atmosphere on sonochemical Wurtz coupling of 1-bromopentane.

One explanation for these differences in rate could be the difference in the polytropic ratio of the gases [15]; a bubble filled with a gas of high polytropic ratio will generate higher temperatures and pressures on implosion. Carbon dioxide has the lowest polytropic ratio of the other gases used and produced the lowest yield and rate of reaction. However, given the nature of the Wurtz reaction (see below), the effect of the gas is more likely to be explained

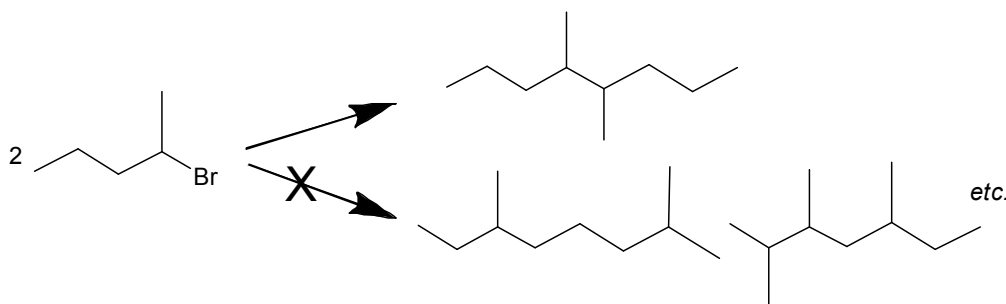
in terms of chemical reactivity. Oxygen will act as a free radical scavenger and so any radical based reaction will be partially quenched when run under oxygen or air. Carbon dioxide is known to react with lithium and its salts so much of the lithium present in our system could have reacted with carbon dioxide deactivating it to coupling. [16, 17]

Further experiments were carried out while varying the stoichiometric equivalents of lithium. As shown in Figure 3, using two equivalents of lithium instead of one had little effect on the rate of bromopentane consumption. When 0.75 eq. was used, the reaction was 63% complete and no further consumption of bromopentane took place after 35 minutes; the corresponding values were 28% and 30 minutes respectively when 0.5 eq. was used. This indicates that the availability of lithium is not rate limiting as long as sufficient is available.



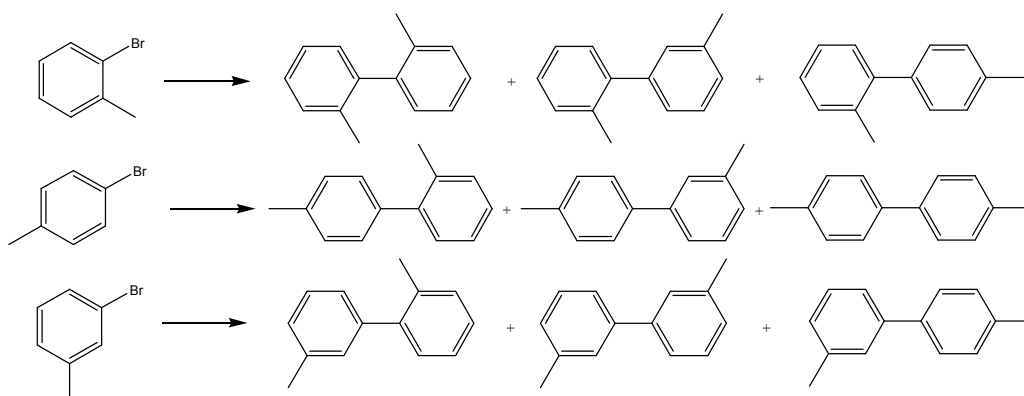
**Figure 3.** Effect of lithium quantity on sonochemical Wurtz coupling of 1-bromopentane

In order to determine whether the formation of a single product was a feature of alkyl systems (in contrast to aromatics), coupling reactions were conducted using 1- and 2-bromopentane, 1-bromo-3-methylbutane, 2-bromo-2-methylbutane, 1-bromo-2,2-dimethylpropane. In each case, only a single product was formed resulting from the coupling of both fragments at the position of the bromine atom. (Scheme 2).



**Scheme 2.** Coupling of alkyl bromides. Only a single isomer is observed.

The formation of a single product is in complete contrast to the bromoaryls studied by Osborne et al [7] and by Price and Clifton [8] (Scheme 3) where mixtures of isomers were produced. However, in each case, the reactions proceeded via a radical intermediate. Aryl radicals are generally more stable and hence less reactive than alkyl radicals and we postulate that the intermediates produced during coupling of aryl bromides are sufficiently long-lived for rearrangement to take place. In contrast, in the more reactive alkyl radicals, no rearrangement can take place prior to coupling and so only a single product is seen.



**Scheme 3.** Sonochemical coupling of bromotoluenes [8]. Each of the possible isomers is formed in one ring.

Another significant difference between these systems was that coupling of bromobenzene was found to follow second order kinetics (rate constant,  $k = 0.01 \text{ dm}^3 \text{ mmol}^{-1} \text{ min}^{-1}$ ) while that of the bromoalkanes was found to follow first order kinetics ( $k = 0.07 \text{ min}^{-1}$  and  $k = 0.04 \text{ min}^{-1}$  for the 1- and 2- isomers respectively). This adds further evidence to our suggestion of more reactive alkyl radical intermediates, the argument being as follows. The generally accepted mechanism [18] of the reaction initially involves an electron transfer from



the metal to produce lithium bromide and an alkyl radical followed by a second electron transfer to form an alkyl anion.



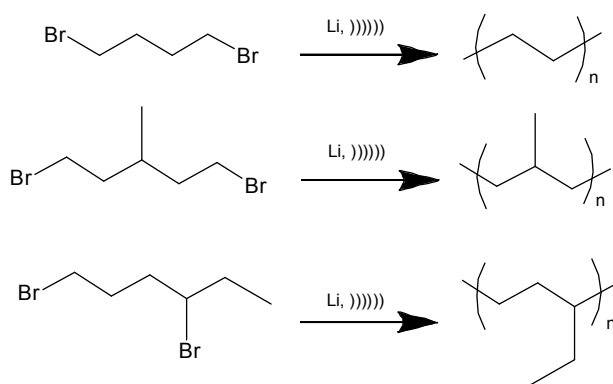
The coupled product then arises from displacement of a bromide ion from a second molecule of alkyl bromide, usually in a  $\text{S}_{\text{N}}2$  reaction.



The overall kinetics of the process will therefore depend on the relative rate constants for the steps. Where  $k_2$  is relatively faster (i.e. the radical is short lived),  $k_3$  will be the rate limiting step and the overall reaction will be second order; conversely, if  $k_2$  is the slow step then the observed reaction order will be one (pseudo-first).

In a related experiment, a “cross coupling” between bromobenzene and bromopentane was attempted. Analysis of the NMR spectra suggested cross reaction had occurred (aromatic proton to alkyl proton coupling was seen in a COSY experiment to differentiate from a mixture of pentane and benzene) but the recovered yield of pentyl benzene was only approx. 10%, the majority products being those from the homocoupling.

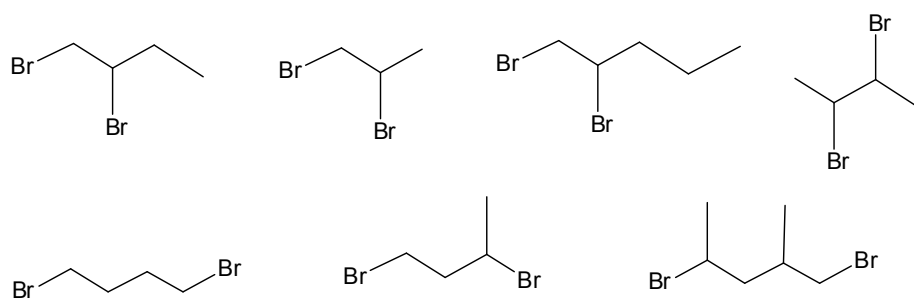
Since mono-brominated aryl and alkyl compounds undergo efficient Wurtz coupling, the possibility of forming polymeric materials from dibrominated compounds (Scheme 4) was investigated using 1,4-dibromobenzene, 1,4-dibromobutane and 1,6-dibromohexane.



**Scheme 4.** Potential coupling of alkyl dibromides to give poly(alkene)s.

The coupling of 1,4-dibromobenzene led to a sticky brown “toffee-like” material which was found by GPC to have an average relative molar mass of 716 corresponding to an oligomer with around 9 repeat units. NMR suggested that a short chain polyphenylene-like material had been formed although the coupling was not exclusively at the 1,4- positions, as might be expected from the results on monosubstituted aryls. Similarly 1,6-dibromohexane and 1,4-dibromobutane coupled under the same conditions yielded white solids which had molar masses of 516 and 464 mass units respectively. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR of both samples were identical and consistent with the spectra of long chain alkanes or polyethylene with no significant branching or alkyl groups due to rearrangement.

Coupling of a series of 1,3- and 1,2- dibrominated alkanes shown in Scheme 5 was attempted. Significantly, the 1,2- isomers did not react even after prolonged sonication times whereas the 1,3- isomers reacted but formed a complex mixture of products containing linear and substituted oligomers. Only the isomers with terminal substituents gave clean products.



**Scheme 5.** Alkyl dibromides for potential sonochemical coupling

The short chain lengths of the oligomers produced by these reactions was disappointing but may well be a consequence of the rapidly decreasing solubility as the alkane chain length increases. In order to counter the potential insolubility of long chain polyalkanes in THF at 25 °C coupling of 1,6-dibromohexane in decalin at 70°C (polyethylene being soluble under these conditions) was attempted. However no reaction occurred and only the starting materials were recovered. It may be the solvent vapour pressure was too high under these conditions to allow sufficient cavitation to influence reaction at the metal surface.. From the parallel with silicon-based materials [19, 20], it may also be that a stronger reducing agent such as sodium is needed, although poly(organosilanes) are often more soluble than polyethylene and so may form more easily.

The results can be rationalised by considering the mechanism outlined above. The initial electron transfer step takes place at or near to the metal surface. The metal surface would rapidly become covered with a layer of lithium bromide, preventing access of further alkyl halide. Using ultrasound 'cleans' the surface by removing this passivating layer and hence allows the reaction to proceed, explaining why ultrasound is useful in this reaction. This process becomes more difficult as the alkyl halide becomes bulkier. It is known [18] that the side reaction to form an alkene becomes more prevalent with bulkier substituents at the halogen containing carbon due to radical stabilisation and the higher activation energy for the second substitution reaction favouring an elimination pathway. In the 1,2- dibromo alkanes, there may not be sufficient conformational flexibility for both bromine atoms to approach the surface. Our results suggest that for coupling to occur the bromines must be separated by at least one methylene group if they are to interact effectively with the surface.

#### **4, Conclusion**

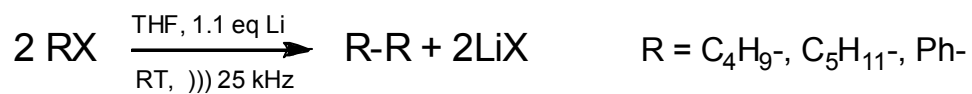
It has been shown that the Wurtz type coupling of bromoalkyls is possible and follows a mechanism involving radical intermediates. No migration of the radical position occurs, in contrast to the findings in aromatic systems. The process can also be used with dibrominated compounds although the bromines must be separated by at least two carbon atoms.

## 5. References

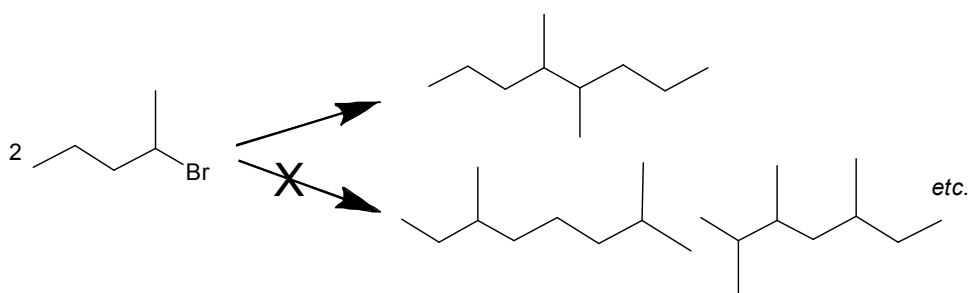
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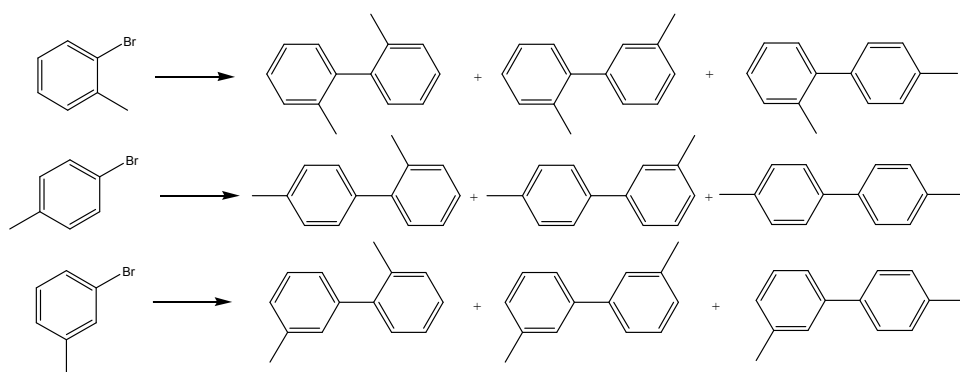
## Figures and Schemes



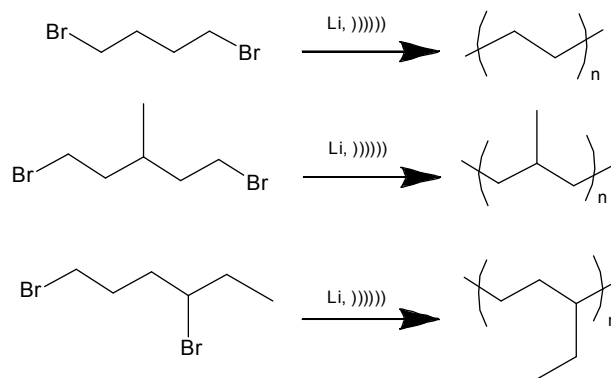
**Scheme 1.** Sonochemical Wurtz coupling



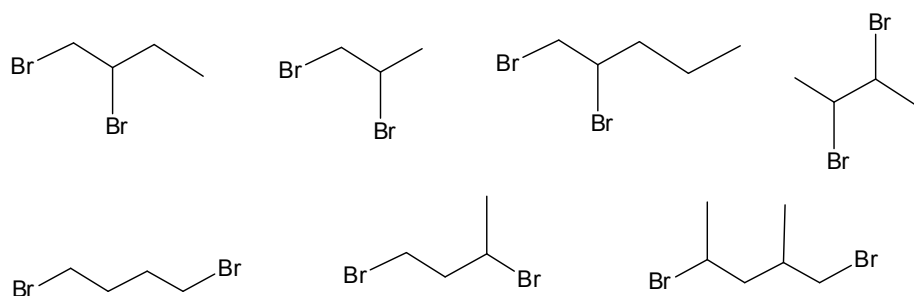
**Scheme 2.** Coupling of alkyl bromides. Only a single isomer is observed.



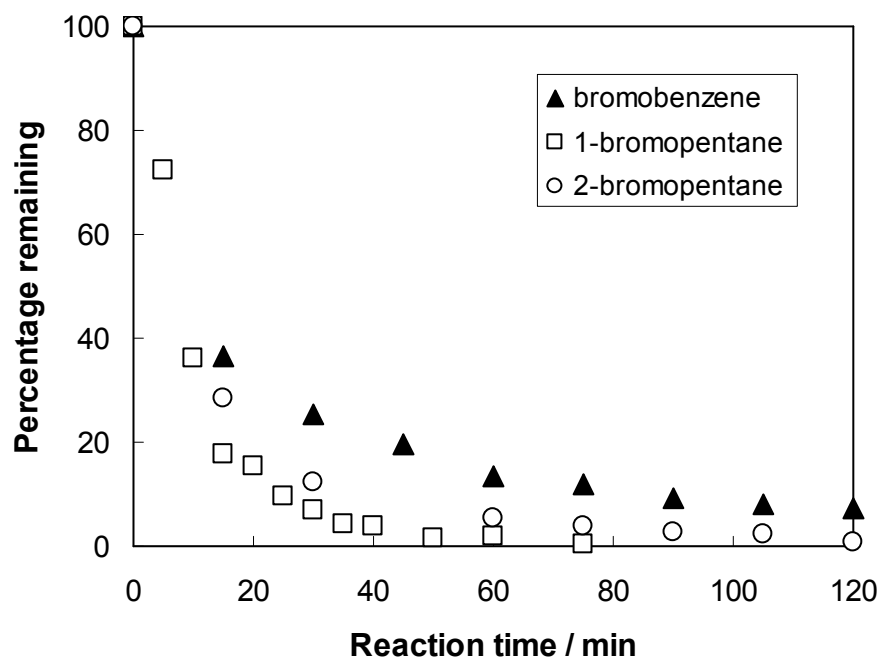
**Scheme 3.** Sonochemical coupling of bromotoluenes [8]. Each of the possible isomers is formed in one ring.



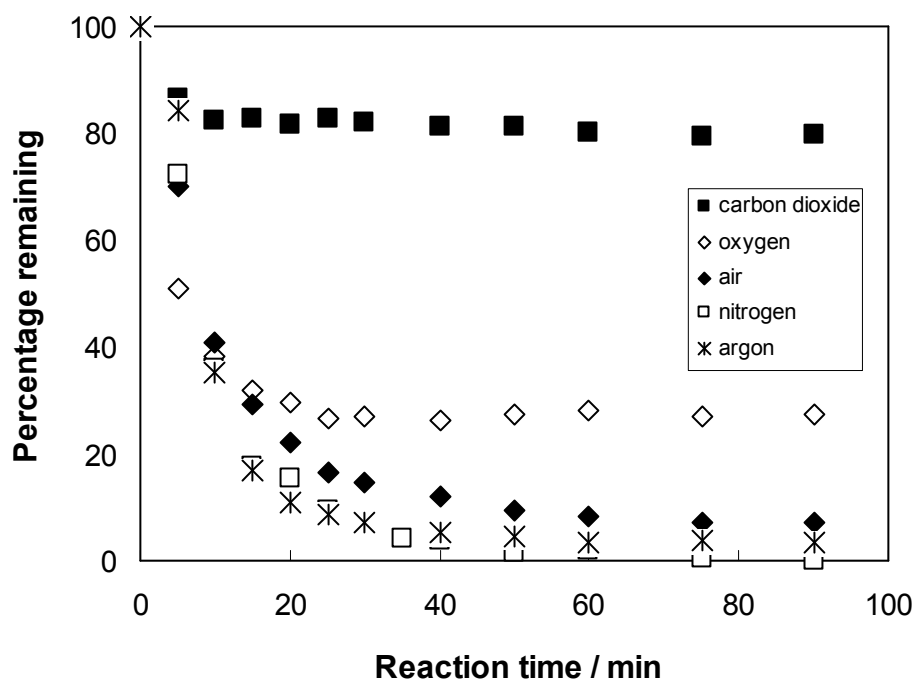
**Scheme 4.** Potential coupling of alkyl dibromides to give poly(alkene)s.



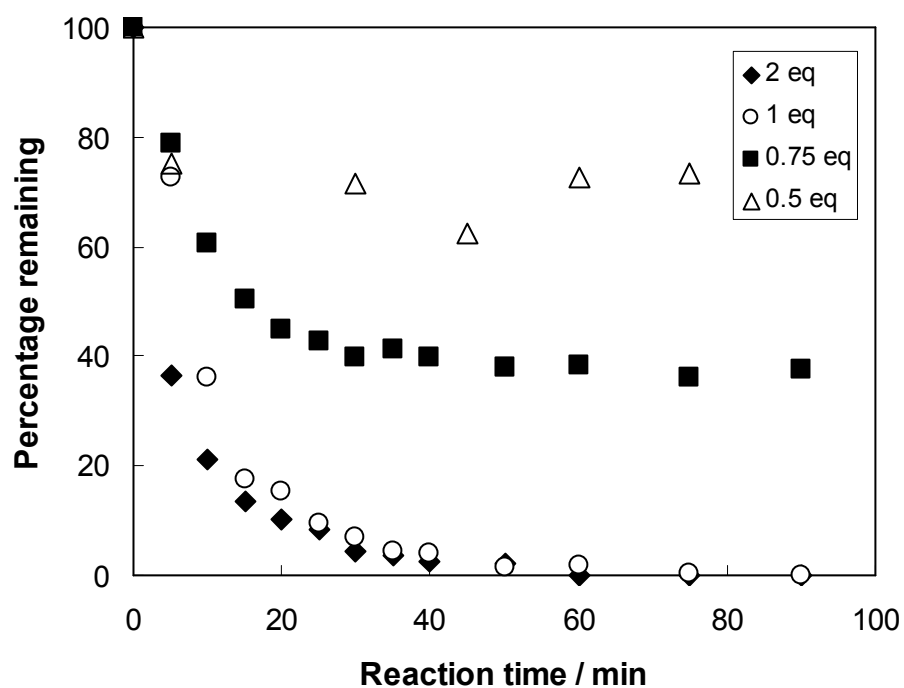
**Scheme 5.** Alkyl dibromides for potential sonochemical coupling



**Figure 1.** Consumption of bromobenzene and bromopentanes during sonochemical Wurtz coupling using lithium.



**Figure 2.** Effect of gaseous atmosphere on sonochemical Wurtz coupling of 1-bromopentane.



**Figure 3.** Effect of lithium quantity on sonochemical Wurtz coupling of 1-bromopentane